

A II

37. (Once amended) The invention of Claim 6, wherein said composition further comprises a component selected from the group consisting of an excipient, an adjuvant and a carrier.

38. (Once amended) The invention of Claim 6, wherein said therapeutic compound is selected from the group consisting of a naked nucleic acid vaccine and a recombinant cell vaccine.

REMARKS

Claims 4, 5, 7, 9, 15, 20, 22, 24, 28-36 have been canceled. Claims 1-3, 6, 8, 10-14, 16-19, 21, 23, 25-27, 37 and 38 have been amended to comply with the election of Group II for further prosecution. Applicants note that these amendments merely cancel Claims not falling within Group II, IV, XXIII or XXV and amend the remaining Claims to remove SEQ ID NO's outside the SEQ ID NO's of the above-mentioned Groups defined by the Examiner.

Accordingly, Applicants contend no new matter has been entered into the Application.

I. Group Election

In response to the Restriction Requirement dated June 13, 2002, Applicants provisionally elect to prosecute Group II with traverse. Applicants note this elections is made solely in the interest of expediting prosecution of this Application and Applicants reserve the right to traverse division between Groups I and III-XLV and division between species in subsequent divisional filings. Applicants also reserve the right to file divisional Applications relating to these claims without the need to file a terminal disclaimer.

The Examiner has restricted the present Application into 45 different groups related to proteins, nucleic acid molecules, antibodies, mimetopes, methods of regulating T-cell responses and methods of identifying inhibitory compounds, all further relating to either canine B7-1, canine B7-2, canine CTLA4, feline B7-1, feline B7-2 and feline CTLA4 molecules. Group II, consisting of Claims 1-3, 6, 8, 10-14, 16-21, 23, 25, 26 and 37-38, is drawn to canine B7-2 nucleic acid molecules, compositions thereof, methods of producing the proteins encoded by the nucleic acids, as well as recombinant molecules, vectors and host cells comprising these molecules. B7-2 nucleic acid molecules of Group II Claims include SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:19, and SEQ ID NO:20. Proteins encoded by B7-2 nucleic acid molecules referenced in Group II

Claims include SEQ ID NO:7 and SEQ ID NO:17. A chart relating the relevant SEQ ID NO's to the relevant molecules is shown below for the Examiner's convenience.

SEQ ID NO:	TYPE	MOLECULE NAME	DESCRIPTION
Group II - canine B7-2 nucleic acid molecules			
6	DNA	nCaB7-2 ₁₈₉₇	FWD full length clone
7	Protein	PcaB7-2 ₃₂₉	Translation of 6 ORF
8	DNA	nCaB7-2 ₁₈₉₇	Comp full length
9	DNA	nCaB7-2 ₉₈₇	FWD coding sequence
10	DNA	nCaB7-2 ₉₈₇	Comp coding sequence
16	DNA	nCaB7-2s ₁₇₉₅	FWD full length variant
17	Protein	PCaB7-2s ₂₈₀	Translation of 16 ORF
18	DNA	nCaB7-2s ₁₇₉₅	Comp variant
19	DNA	nCaB7-2s ₈₄₀	FWD coding sequence
20	DNA	nCaB7-2s ₈₄₀	Comp coding sequence
Group IV - feline B7-2 nucleic acid molecules			
25	DNA	nFeB7-2 ₂₈₃₀	FWD full length
26	Protein	PFeB7-2 ₃₃₂	Translation of 25 ORF
27	DNA	nFeB7-2 ₂₈₃₀	Comp full length
28	DNA	nFeB7-2 ₉₉₆	FWD coding sequence
29	DNA	nFeB7-2 ₉₉₆	Comp coding sequence
30	DNA	nFeB7-2 ₅₀₉	PCR clone-1-nucleotides 662-1170 of 25 -FWD
31	Protein	PFeB7-2 ₁₆₉	Translation of 30
32	DNA	nFeB7-2 ₅₀₉	Comp PCR clone
33	DNA	nFeB7-2s ₃₅₉	FWD PCR clone-2
34	Protein	PFeB7-2s ₁₁₉	Translation of 33
35	DNA	nFeB7-2s ₃₅₉	Comp

II. Restriction Between Groups II and IV

M.P.E.P § 803.04 states that although independent and distinct inventions should normally be restricted by an Examiner, in the case of nucleotide sequences, the requirements of 37 C.F.R. § 1.141 are partially waived and a reasonable number of nucleotide sequences that encode different proteins can be examined together. It has been determined that normally ten sequences constitute a reasonable number for examination purposes. Groups II and IV describe nucleic acid sequences encoding two closely related proteins, *i.e.* canine B7-2 and feline B7-2. The canine and feline B7-2 are approximately 90% identical at the nucleotide level and approximately 80% identical at the amino acid level as determined using SEQ ID NO's 6 and 9 and the NIH BLAST program set with default parameters. Additionally, the instant Application contains evidence that the canine B7-2 protein is capable of stimulating proliferation of canine T-

cells. Further, the human B7-2 protein, which is approximately 60% identical to the canine B7-2 protein, has also been shown to stimulate T-cell proliferation. This evidence suggests the feline protein, being much more closely related to the canine B7 protein than is the human B7 protein, will also have the same function. Since the sequences of the canine and feline genes and proteins are so closely related and are likely to possess the same activity, Applicants respectfully submit that a thorough search for the subject matter of Group II would be sufficient to enable the examination of the Claims of Group IV without constituting an undue burden for the Examiner. While the number of sequences in these groups are in excess of ten, Applicants note that many of the sequences within each Group are merely fragments of larger sequences (e.g. SEQ ID NO.'s 6 & 9) and the sequences of these fragments are identical, over their length, with the sequence of the parent molecule. These fragments may be considered to encode the same protein as the parent and therefore would not constitute an independent invention requiring an independent search. M.P.E.P § 803.04 Therefore, due to the overlapping and identical nature of the fragments, the number of distinct sequences that must be searched and examined would be reduced. In light of the above, Applicants respectfully request rejoinder of Groups II and IV.

II. Restriction Between Groups II and IV and Groups XXIII and XXV

Applicants traverse the restriction between Groups II and XXIII to the extent that Group XXIII recites the subject matter of Group II, and, accordingly, Applicants also traverse the restriction between Groups IV and XXV if Groups II and IV are rejoined. Applicants submit that the subject matter of these Groups is sufficiently small and is so closely related, that a thorough search for Group II or Group IV should also include the subject matter of Group XXIII or Group XXV. Specifically, the Claims of Group XXIII are drawn to a method of regulating a T-cell mediated immune response using the B7-2 nucleic acids, or compositions thereof, of Group II. Applicants emphasize the method defined by Group XXIII requires the use of B7-2 nucleic acids of Group II and, therefore, a search for the subject matter of either Group would be sufficient to examine the Claims of the related Group. Further, because the method of Group XXIII cannot be practiced without the composition(s) of Group II, Applicants submit these Groups do not describe independent inventions as described in the M.P.E.P §802.01 and therefore request rejoinder of these Groups. If the Examiner rejoins Groups II and XXIII, Group XXV should also be rejoined and examined with the subject matter of Group IV under the same reasoning.

In view of the foregoing arguments, Applicants respectfully request that the Examiner withdraw the restrictions between Groups II, IV, XXIII and XXV. Applicants reserve the right to traverse restrictions between any of the Groups in subsequent divisional applications. Applicants also reserve the right to file divisional applications relating to any and all of these Groups without the necessity of filing a terminal disclaimer.

In any event, if the elected claims of Group II are allowable, Applicants reserve their right to amend the claims of Group XXIII to be commensurate in scope with the product claims of Group II, and to request that the claims of Groups XXIII that depend from or otherwise include all the limitations of the allowable product be rejoined and examined for patentability. *In re Brouwer*, 37 USPQ2d 1663 (Fed. Cir. 1996); *In re Ochiai*, 37 USPQ2d 1127 (Fed. Cir. 1995). Furthermore, if the elected claims of Group IV are rejoined and found allowable, Applicants reserve their right to amend the claims of Group XXV to be commensurate in scope with the product claims of Group IV, and to request that the claims of Groups XXV that depend from or otherwise include all the limitations of the allowable product be rejoined and examined for patentability.

Respectfully submitted,

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VERSION WITH MARKINGS SHOWING CHANGES

Claim 4, 5, 7, 9, 15, 20, 22, 24, 28-36 and 39 have been canceled.

1. An isolated nucleic acid molecule selected from the group consisting of: a nucleic acid molecule having a nucleic acid sequence that is at least about 80 percent identical to a nucleic acid sequence selected from the group consisting of [SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5,] SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, [SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15,] SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, or a fragment thereof having at least about 12 nucleotides[; a nucleic acid molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39, and SEQ ID NO:40; and a nucleic acid molecule having a nucleic acid sequence that is at least about 90 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, or a fragment thereof having at least about 12 nucleotides].

2. An isolated nucleic acid molecule selected from the group consisting of:
 - (a) a nucleic acid molecule having a nucleic acid sequence encoding a B7 protein selected from the group consisting of :[a protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:2, a protein comprising an epitope of said protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:2,] (i) a protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:7, (ii) a protein comprising an epitope of said protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:7, [a protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:12, a protein comprising an epitope of said protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:12,] (iii) a protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:17, (iv) a protein comprising an epitope of said protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:17, (v) a protein having an

amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:26, (vi) a protein comprising an epitope of said protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:26, (vii) a protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:34, and (viii) a protein comprising an epitope of said protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:34[, and a protein having amino acid sequence SEQ ID NO:37]; and

(b) a nucleic acid molecule comprising a complement of any of said nucleic acid sequences set forth in (a)[;

(c) a nucleic acid molecule having a nucleic acid sequence encoding a CTLA4 protein selected from the group consisting of: a protein having an amino acid sequence that is at least about 90 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:42 and SEQ ID NO:47; and a protein comprising an epitope of said protein having an amino acid sequence that is at least about 90 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:42 and SEQ ID NO:47; and

(d) a nucleic acid molecule comprising a complement of any of said nucleic acid sequences set forth in (c); wherein said B7 protein elicits an immune response against a naturally-occurring B7 protein, and wherein said CTLA4 protein elicits an immune response against a naturally-occurring CTLA4 protein].

3. An isolated nucleic acid molecule selected from the group consisting of a nucleic acid molecule that encodes a naturally-occurring soluble mammalian B7-2 protein and a nucleic acid molecule comprising a complement of said nucleic acid molecule that encodes said protein.

6. A therapeutic composition that, when administered to an animal, regulates T cell mediated immune responses in said animal, said therapeutic composition comprising [a therapeutic compound selected from the group consisting of: an isolated protein comprising a B7 protein, wherein said B7 protein is selected from the group consisting of a protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:2, a protein comprising an epitope of said protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:2, a protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ

ID NO:7, a protein comprising an epitope of said protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:7, a protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:12, a protein comprising an epitope of said protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:12, a protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:17, a protein comprising an epitope of said protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:17, a protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:26, a protein comprising an epitope of said protein having an amino acid sequence that is at least about 60 percent identical to the amino acid sequence SEQ ID NO:26, a protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:34, a protein comprising an epitope of said protein having an amino acid sequence that is at least about 80 percent identical to the amino acid sequence SEQ ID NO:34, a protein having amino acid sequence SEQ ID NO:37, an isolated naturally-occurring soluble B7 protein; a mimotope of any of said B7 proteins; a multimeric form of any of said B7 proteins; an isolated protein comprising a CTLA4 protein selected from the group consisting of: a protein having an amino acid sequence that is at least about 90 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:42 and SEQ ID NO:47; and a protein comprising an epitope of said protein having an amino acid sequence that is at least about 90 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:42 and SEQ ID NO:47; a mimotope of any of said CTLA4 proteins; a multimeric form of any of said CTLA4 proteins;] an isolated nucleic acid molecule selected from the group consisting of: a nucleic acid molecule having a nucleic acid sequence that is at least about 80 percent identical to a nucleic acid sequence selected from the group consisting of [SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5,] SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, [SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15,]SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, and SEQ ID NO:35[; a nucleic acid molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39, and SEQ ID NO:40; and a nucleic acid molecule having a nucleic acid sequence that is at least about 90 percent identical to

a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, and SEQ ID NO:50; an isolated antibody that selectively binds to any of said B7 proteins; an inhibitor of B7 protein activity identified by its ability to inhibit the activity of any of said B7 proteins; an isolated antibody that selectively binds to any of said CTLA4 proteins; and an inhibitor of CTLA4 protein activity identified by its ability to inhibit the activity of any of said CTLA4 proteins].

8. A method to produce a [protein selected from the group consisting of a] B7 protein [and a CTLA4 protein], said method comprising culturing a cell capable of expressing said protein, said protein being encoded by a nucleic acid molecule selected from the group consisting of: (a) a nucleic acid molecule having a nucleic acid sequence that is at least about 80 percent identical to a nucleic acid sequence selected from the group consisting of [SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5,] SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, [SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15,] SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, or a fragment thereof having at least about 18 nucleotides, wherein said fragment encodes an epitope[; a nucleic acid molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39, and SEQ ID NO:40; a nucleic acid molecule having a nucleic acid sequence that is at least about 90 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, [or] and a fragment thereof having at least about 18 nucleotides, wherein said fragment encodes an epitope;] ;and (b) a nucleic acid molecule that encodes a naturally-occurring soluble mammalian B7 protein.

10. The invention of Claims 1,2, [or] 6[-] or 8, wherein said nucleic acid molecule comprises a nucleic acid sequence that encodes a [protein selected from the group consisting of a]B7 protein [and a CTLA4 protein].

11. The invention of Claims 1,2, [or] 6[-] or 8, wherein said nucleic acid molecule encodes a protein that elicits an immune response against a [protein selected from the group consisting of a] naturally-occurring B7 protein [and a naturally-occurring CTLA4 protein].

12. The invention of Claims 1,2, [or] 6[-] or 8, wherein said nucleic acid molecule is selected from the group consisting of: a nucleic acid molecule comprising a nucleic acid molecule selected from the group consisting of [nCaB7-1₂₈₃₀, nCaB7-1₁₃₈₅, nCaB7-1₉₁₂,] nCaB7-2₁₈₉₇, nCaB7-2₉₈₇, [nCaB7-1s₁₀₂₄, nCaB7-1s₇₀₅,] nCaB7-2s₁₇₉₅, nCaB7-2s₈₄₀, nFeB7-2₂₈₃₀, nFeB7-2₉₉₆, [nCaB7-1s₁₀₁₀,] nCaB7-2₉₂₁, [nCaB7-1s₆₀₃,] nCaB7-2s₇₇₄, nFeB7-2₉₁₈, nFeB7-2₅₀₉, nFeB7-2s₃₅₉, nCaCTLA4₁₈₅₆, nCaCTLA4₆₇₂, nFeCTLA4₁₈₈₃, and nFeCTLA4₆₇₂; and a nucleic acid molecule consisting of a nucleic acid molecule selected from the group consisting of nFeB7-1s₅₉₄ and nFeB7-1s₅₁₉.

13. The invention of Claims 1,2, [or] 6[-] or 8, wherein said nucleic acid molecule is selected from the group consisting of: a nucleic acid molecule comprising a nucleic acid sequence that encodes a protein having an amino acid sequence selected from the group consisting of : (a) [SEQ ID NO:2,]SEQ ID NO:7, [SEQ ID NO:12,]SEQ ID NO:17, SEQ ID NO:26, SEQ ID NO:31[,] and SEQ ID NO:34[, SEQ ID NO:42, and SEQ ID NO:47]; and (b) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule encoding a protein having an amino acid sequence selected from the group consisting of [SEQ ID NO:2,]SEQ ID NO:7, [SEQ ID NO:12,] SEQ ID NO:17, SEQ ID NO:26, SEQ ID NO:31[,] and SEQ ID NO:34[, SEQ ID NO:42, and SEQ ID NO:47; a nucleic acid molecule consisting of a nucleic acid sequence that encodes a protein having amino acid sequence SEQ ID NO:37; and a nucleic acid molecule consisting of an allelic variant of a nucleic acid molecule that encodes a protein having amino acid sequence SEQ ID NO:37].

14. The invention of Claims 1,2, [or] 6[-] or 8, wherein said nucleic acid molecule is selected from the group consisting of: (a) a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of [SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5,] SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, [SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15,] SEQ ID NO:16, SEQ ID NO:18, SEQ ID

NO:19, SEQ ID NO:20, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, and SEQ ID NO:35, [SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, and SEQ ID NO:50]; and (b) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule comprising any of said nucleic acid sequences.

16. The invention of Claims 1-3 [or] , 6[-] or 8, wherein said nucleic acid molecule comprises an oligonucleotide.

17. A recombinant molecule comprising a nucleic acid molecule as set forth in Claims 1-3 [or] , 6[-] or 8, operatively linked to a transcription control sequence.

18. A recombinant virus comprising a nucleic acid molecule as set forth in Claims 1-3 [or] , 6[-] or 8.

19. A recombinant cell comprising a nucleic acid molecule as set forth in Claims 1-3 [or] , 6[-] or 8.

21. The nucleic acid molecule of Claim 3, wherein said nucleic acid molecule comprises a nucleic acid sequence encoding a naturally-occurring soluble B7-2 protein having extracellular and intracellular domains but lacking at least a portion of a transmembrane domain sufficient to produce a soluble protein upon translation of said nucleic acid molecule in a suitable host cell.

23. The nucleic acid molecule of Claim 3, wherein said naturally-occurring soluble mammalian B7-2 protein is capable of binding to a protein selected from the group consisting of CD28 and CTLA4.

25. The nucleic acid molecule of Claim 3, wherein said naturally-occurring soluble mammalian B7-2 protein is capable of delivering a co-stimulatory signal to a helper T cell sufficient to stimulate cytokine secretion by said helper T cell.

26. The nucleic acid molecule of Claim 1-3 [or] , 6[-] or 8, wherein said nucleic acid molecule is selected from the group consisting of a canine nucleic acid molecule and a feline nucleic acid molecule.

27. The invention of Claim[s 4 or]6[-9], wherein said protein, when administered to an animal, elicits an immune response against [a protein selected from the group consisting of a B7-1 protein,] a B7-2 protein [and a CTLA4 protein].

37. The invention of Claim 6 [or Claim 7], wherein said composition further comprises a component selected from the group consisting of an excipient, an adjuvant and a carrier.

38. The invention of Claim 6 [or Claim 7], wherein said therapeutic compound is selected from the group consisting of a naked nucleic acid vaccine and a recombinant cell vaccine.